REMARKS

Claims 18-34 were previously pending in this application. By this amendment, Applicant is canceling claims 18-34 without prejudice or disclaimer. Applicant maintains the right to pursue the subject matter of any of the canceled claims in one or more continuing applications. Claims 42-62 have been added. Support for the newly added claims can be found in the original claims as filed and on page 19, line 23 through page 20, line 9. As a result, claims 42-62 are pending for examination with claims 42 and 58-60 being independent claims. Although all of the previously rejected claims are herewith canceled, Applicant wishes to address the Examiner's concerns of the previously rejected claims in light of the newly added claims. Applicant respectfully thanks the Examiner for the indication that claims 30-32 were allowable. The references and cases cited herein are provided with the exception of Janeway et al., which was previously cited by the Examiner. No new matter has been added.

Objections to Claims 23-25

The Examiner in his Advisory Action has objected to claims 23-25 as being dependent upon a rejected claim. The Examiner suggests that the claims would be allowable if rewritten in independent form. For the reasons provided below Applicant traverses the objection of these claims and maintain that rewriting claims 23-25 in independent form would not have been necessary.

Rejections Under 35 U.S.C. §112

The Examiner had previously rejected claims 18-29 and 33-34 under 35 U.S.C. §112, first paragraph. In the Examiner's Final Office Action, these claims were rejected as containing subject matter that was not described in such a way as to reasonably convey to one skilled in the art that the inventors at the time the application was filed had possession of the claimed invention.

The Applicant respectfully disagrees. The specification clearly exemplifies peptides that bind human mannose binding lectin (MBL) in a way sufficient to satisfy the written description requirement. These peptides include the monoclonal antibodies produced by hybridoma cell line 3F8 deposited under ATCC Accession No. HB-12621, hybridoma cell line 2A9 deposited under

ATCC Accession No. HB-12620 and hybridoma cell line hMBL1.2 deposited under ATCC Accession No. HB-12619. The peptides also include fragments of the deposited antibodies discussed in the specification on, for example, page 18 and inherently disclosed by the deposit of the antibodies in a public depository. These fragments include the antigen binding portions of the antibodies, such as the complementarity determining regions (CDRs) of the heavy and light chains of these antibodies. The sequence of the antibodies, and likewise fragments of the antibodies, are also necessarily provided by the deposit of the three hybridomas identified in Applicant's specification.

The specification further provides peptides that have the sequence of a CDR region with a conservative substitution therein (see, for example, page 19, line 23 through page 20, line 9). Conservative substitutions are clearly defined in the specification and are identifiable to one of ordinary skill in the art. Therefore, with the structure of the CDR3 regions provided in the specification and the limited variation of conservatively substituted versions of these CDR3 regions, the peptides of the invention are sufficiently disclosed with "sufficiently detailed, relevant identifying characteristics". Enzo Biochem v. Gen-Probe, 323 F.3d 956, 964 (Fed. Cir. 2002). Furthermore, the peptides of the claims must also possess the ability to bind human MBL. Although Applicant maintains that the sequences of the CDR3 regions inherently provided by the deposited antibodies as well as the defined conservative substitutions provide the necessary identifying characteristics of the genus of peptides, Applicant further discloses necessary functional characteristic of the peptides of the claims, i.e., their binding to human MBL. Assays for assessing the disclosed functional characteristics are also well known in the art and are provided by Applicant.

Such a written description as outlined above is more than sufficient to satisfy the written description requirement. The genus of the peptides that have a CDR3 region as provided by the deposited antibodies or conservatively substituted variants of these CDR3 regions do not have substantial variation. All of the variants must possess MBL binding activity and have the sequence of the CDR3 region of the deposited antibodies or conservative substitutions therein. The specification clearly provides the necessary structure and functional characteristics adequate to satisfy the written description requirement. It should be noted that the limitation that the substitutions are conservative necessarily limits the variability of the peptides of the claims to a set that is easily recognizable to one of ordinary skill in the art. One skilled in the art, therefore,

would conclude that the Applicant was in possession of the necessary common characteristics possessed by the members of the genus of human MBL binding peptides with the specific CDR3 regions or conservative substitutions therein.

Furthermore, it has been recognized that a genus of antibodies can be claimed by the recitation of an adequately characterized antigen. Applicant asserts that because human MBL is just such a characterized antigen claims to peptides that bind thereto likewise meet the written description requirement. In Noelle v. Lederman, the court determined that claims to antibodies that bind to a particular antigen satisfy the written description requirement if the antigen is well characterized. Noelle v. Lederman, --- F.3d ---, 2004 WL 77931 (Fed. Cir. 2004). In the court's discussion of the written description requirement ([4]) the following was stated: "Therefore, based on our past precedent, as long as an applicant has disclosed a '*fully characterized* antigen,' either by its structure, formula, chemical name, or physical properties, or by depositing the protein in a public depository, the applicant can then claim an antibody by its binding affinity to that described antigen." Applicant asserts that those of skill in the art are likewise able to easily produce and screen human MBL peptides that contain a CDR3 region of one of the deposited antibodies described in the specification or a conservatively substituted variant thereof for their ability to bind the fully characterized antigen, human MBL (see, e.g., Ezekowitz U.S. Patent 5,270,199 issued December 14, 1993).

Accordingly, Applicant respectfully maintains that the rejection of claims 18-29 and 33-34 under 35 U.S.C. §112, first paragraph should have been withdrawn.

The Examiner had also previously rejected claims 18-29 and 33-34 under 35 U.S.C. §112, first paragraph, as being not sufficiently enabled by the specification so that one skilled in the art was able to make the invention commensurate with the scope of the claims.

As argued previously, Applicant asserts that one of ordinary skill in the art is adequately enabled to make and use the peptides of the claims. With the guidance provided by the instant specification and the high level of skill in the art, Applicant maintains that one of ordinary skill in the art would need only use routine experimentation to make and use the peptides of the claims and, therefore, be able to practice the claimed invention without undue experimentation.

For the level of experimentation to be undue, it must be demonstrated that the experimentation is more than that typically engaged in in the art. Requiring complex or even a

large amount of experimentation is not sufficient to make it undue, if the art routinely engages in this level of experimentation. As argued above, the sequences and various fragments of the antibodies are inherently provided by the deposit of the antibodies in a public depository. With the deposited antibodies, one of skill in the art could easily produce the CDR3 regions, the antigen binding fragments of the antibodies or the whole antibodies themselves to make peptides that fall within the scope of the claims. Additionally, one of ordinary skill in the art would use routine experimentation to produce conservatively substituted CDR3 regions and to assess the function of the peptides produced (e.g., with binding assays and competition assays such as those provided on pages 16-17 of the specification). Based on the materials and guidance provided one of ordinary skill in the art would be reasonably expected to produce peptides that bind human MBL and contain the CDR3 regions of the deposited antibodies or their conservatively substituted variants. Such a reasonable expectation is sufficient to satisfy the enablement requirement.

The Examiner is reminded that the level of skill in the art is very high, and as such, one of ordinary skill in the art would not only be able to easily make conservatively substituted versions of the CDR3 regions provided but would also be able to identify such conservatively substituted versions. The Examiner is reminded that the question regarding enablement is merely whether the disclosure enables one of skill in the art to produce the peptides of the claims. Applicant asserts that this is the case. The ease with which routine methods can be employed to allow for the production of numerous peptides that contain, for example, CDR3 regions or conservatively substituted CDR3 regions and to assess the binding characteristics of these peptides speaks directly to the instant specification's satisfaction of the enablement requirement.

The Examiner has contended that the Applicant has failed to sufficiently enable the invention, in part, due to the teachings of Janeway et al. The Examiner has concluded that because Janeway et al. teach that antibody specificity is determined by the CDR1, CDR2 and CDR3 regions of both antibody chains (heavy and light), the peptides that include the CDR3 regions or conservatively substituted versions thereof are not reasonably expected to bind to human MBL. Applicant, however, again disagrees. As argued previously, the Janeway et al. teachings in no way demonstrate that one of ordinary skill in the art would not be able to make MBL binding peptides that contain the CDR3 regions provided by Applicant based on the

guidance provided by Applicant's specification and the high level of skill in the art. Janeway et al., in fact, describe the importance of the CDR3 regions for antibody specificity. The teaching that other CDRs are involved in antigen binding of a complete antibody is not a teaching that fragments of the antibody, such as fragments as short as a single CDR would fail to bind its specific antigen. The Applicant has taught that a peptide which consists of a CDR3 region would be expected to selectively bind human MBL, and the Examiner has not demonstrated why the Applicant's assertions are not to be believed. That other regions might contribute to the binding of a larger polypeptide is not a teaching that a fragment of the larger polypeptide will fail to bind. Furthermore, as argued above, one of ordinary skill in the art would know how to make a peptide with a CDR3 region and determine the peptide's ability to bind a human MBL epitope using only routine methods known in the art and the teachings of the specification. In addition, it has been demonstrated that antigen-binding synthetic peptides, based on the amino acid sequences of the V_H and V_L domains of an antibody and which include peptides that contain one or more CDR residues, can be produced (Laune, D., et al. Systematic Exploration of the Antigen Binding Activity of Synthetic Peptides Isolated from the Variable Regions of Immunoglobulins. *The Journal of Biological Chemistry*. Vol. 272, No. 49, pp. 30937-30944, 1997; Monnet, C., et al., Synthetic Peptides Derived from the Variable Regions of an Anti-CD4 Monoclonal Antibody Bind to CD4 and Inhibit HIV-1 Promoter Activation in Virus-Infected Cells. *The Journal of Biological Chemistry*. Vol. 274, No. 6, pp. 3789-3796, 1999), and peptides containing the CDR3 region of an antibody also have been shown to be capable of binding antigen (Taub, R., et al., A Monoclonal Antibody against the Platelet Fibrinogen Receptor Contains a Sequence that Mimics a Receptor Recognition Domain in Fibrinogen. *The Journal of Biological Chemistry*. Vol. 264, No. 1, pp. 259-265, 1989; Igarashi, K., et al., Specific Binding of a Synthetic Peptide Derived from an Antibody Complementarity Determining Region To Phosphatidylserine. *J Biochem (Tokyo)*. Vol. 117, No. 2, pp. 452-7, 1995.)

Furthermore, the fact that inactive peptides might be made is irrelevant to the issue of whether the disclosure enables one of skill in the art to make peptides which do bind to human MBL. Applicant maintains that the production of the peptides of the claims was conventional at the time of filing of Applicant's application in view of the knowledge provided in the specification. Similarly to the fact that antibody technology is very mature and advanced, the production and screening of peptide variants is likewise mature and advanced. Certainly because

of the high level of knowledge in the art of producing antibodies, one would not argue that one of ordinary skill in the art would not be enabled to make an antibody to a fully characterized antigen just because it is possible to make antibodies that do not bind the fully characterized antigen. Likewise, one should not argue that just because peptides might be made that do not bind fully characterized human MBL, one is not able to produce peptides that do. Such arguments are not sufficient to defeat the claims from being allowed due to lack of enablement.

In support of the above argument, in In re Marzocchi, the courts found that even though changes can be made which will prevent a compound from having the desired activity, this is not sufficient to assert a rejection for lack of enablement when one of ordinary skill in the art can easily avoid such compounds. In re Marzocchi, 439 F.2d 220, 224 (CCPA 1971). The court stated the following: "It does appear that variation of certain of the secondary factors mentioned by the examiner, such as molecular weight or proportion of ethylene groups, might influence to some degree or even mask the essential 'amine' property of the polyethylene amine or its obviously equally essential compatibility with vinyl polymers. However, we see no basis to conclude that the ready avoidance of this result would not be within the level of ordinary skill in this art." In re Marzocchi, 439 F.2d 220, 224 (CCPA 1971). Similarly, the level of skill in the relevant art of the biological sciences is also very high, and even though peptides might be produced that do not bind human MBL, the highly skilled artisan is reasonably able to avoid such peptides. The highly skilled artisan is also reasonably able to produce peptides with the structural characteristics of the human MBL binding peptides provided by Applicant based on the guidance provided in the Applicant's specification and the knowledge of those in the art.

Accordingly, Applicants respectfully maintain that the rejection of claims 18-29 and 33-34 under 35 U.S.C. §112, first paragraph should also have been withdrawn.

CONCLUSION

In view of the foregoing amendments and remarks, this application should now be in condition for allowance. A notice to this effect is respectfully requested. If the Examiner believes, after this amendment, that the application is not in condition for allowance, the Examiner is requested to call the Applicant's representative at the telephone number listed below.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Respectfully submitted,

Gregory L. Stahl et al., Applicant

By: 

Janice A. Vatland, Reg. No. 52,318
Wolf, Greenfield & Sacks, P.C.
600 Atlantic Avenue
Boston, Massachusetts 02210-2211
Telephone: (617) 646-8000

Docket No. A0752.70001US00
Date: April 23, 2004
x04/23/04x